Aliskiren Achieved Better Control Than Irbesartan

BY MITCHEL L. ZOLER
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NEW ORLEANS — Monotherapy with the direct renin inhibitor aliskiren was more effective at lowering blood pressure in hypertensive patients with metabolic syndrome than the angiotensin-receptor blocker irbesartan in a randomized study with 138 evaluable patients.

Aliskiren monotherapy also resulted in a significantly higher percentage of patients reaching their goal blood pressure, compared with those on irbesartan, Dr. Wilhelm Krone, professor and chairman of the second department of internal medicine at the University of Cologne (Germany), and his associates reported in a poster at the annual scientific sessions of the American Heart Association.

"Chronic activation of the renin system has been implicated in many of the key features of metabolic syndrome," they said. "We hypothesize that the greater blood pressure–lowering effects by aliskiren relative to irbesartan in metabolic syndrome may be the result of more complete renin system inhibition by aliskiren in the kidney and/or adipose tissue. Adipocytes may contribute to blood pressure elevation in obesity-related hypertension through the generation of angiotensin II." They also noted that metabolic syndrome occurs in more than a third of patients with hypertension.

The study was supported by Novartis, which markets aliskiren (Tekturna).

The subjects were aged 40-75 (average 59), 65% were men and 96% were white, and had metabolic syndrome. They all had essential hypertension (systolic pressure of at least 130 mm Hg or diastolic pressure of at least 85 mm Hg) and a waist circumference that met the definition for metabolic syndrome (at least 102 cm in men and 88 cm in women). In addition, they had to either have a plasma triglyceride level of more than 150 mg/dL or a

Early Diastolic Dysfunction Seen in Diabetics

NEW ORLEANS — Preclinical diastolic dysfunction was highly prevalent among patients with diabetes, occurring in 24% of more than 1,700 largely unselected patients in a retrospective study.

Diastolic dysfunction without any initial clinical manifestations in patients with either type 1 or type 2 diabetes also had substantial clinical consequences, leading to a significantly increased rate of both heart failure and all-cause mortality during up to 5 years of follow-up, Dr. Aaron M. From reported at the annual scientific sessions of the American Heart Association.

Dr. From, of the Mayo Clinic in Rochester, Minn., and his associates studied the natural history of preclinical diastolic dysfunction in diabetes patients by reviewing the records of 2,770 patients with either type 1 or type 2 diabetes who were residents of Olmsted County, Minn. and who underwent an echocardiographic examination at the clinic during 1996-2006. A total of 1,794 patients were included in the final analysis.

The average age of these patients was 60, about half were women, their average body mass index was 33 kg/m^2, 86% were hypertensive, 37% had coronary disease, and most had type 2 diabetes.

Using the ratio between the patient's early mitral filling velocity—the E wave—and the mitral annulus velocity—the e' wave—431 (24%) of the 1,784 patients with diabetes had diastolic dysfunction at the time of their echo exam.

Subsequent development of heart failure was identified by finding ICD-9 code 428 in the patient's record. A prior study of Olmsted County patients showed that this code identified 90% of heart failure cases. During up to 5 years of follow-up, the rate of new-onset heart failure was 37% in patients with diastolic dysfunction at baseline and 17% in those without diastolic dysfunction, a statistically significant difference, said Dr. From, who also reported that he and his coauthors had no conflicts of interest related to the study.

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fasting plasma glucose level between 100.8 mg/dL and 126 mg/dL.

Sixty-six were randomized to treatment with aliskiren and 75 were assigned to treatment with irbesartan. The average blood pressure at baseline was 156/94 mm Hg in the aliskiren group and 154/92 in the irbesartan group.

During the first 2 weeks of treatment, patients received either 150 mg of aliskiren once daily or 150 mg irbesartan once daily. After 2 weeks, the daily dosage in both arms was doubled to 300 mg once daily, and that dosage was maintained for an additional 10 weeks.

After a total of 12 weeks of treatment, blood pressure was cut by an average of 13.8/7.1 mm Hg in the 66 aliskiren-treated patients who completed the study and an average of 5.8/2.8 mm Hg in the 72 irbesartan-treated patients who finished the study. The differences in average reduction in both systolic and diastolic blood pressure were statistically significant. The percent of patients reaching the goal blood pressure of less than 135/85 mm Hg was 29% in the aliskiren group and 17% in the irbesartan group, a statistically significant difference.

Both treatments were generally well tolerated, with no serious adverse events in either arm. Neither drug was associated with a significant change in blood glucose or lipid profile and neither led to hyperkalemia or an increase in serum creatinine or blood urea nitrogen.

The study tracked changes in the levels of several biomarkers of inflammation, thrombosis, fibrosis, and oxidative state. No differences were seen between the two drugs for any of these, except that aliskiren therapy led to greater reductions of renin-system biomarkers, and irbesartan raised the level of eotaxin, an inflammatory cytokine. ■

Aspirin No Aid For Metabolic Syndrome

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NEW ORLEANS — Apparently healthy people with a family history of coronary artery disease who also had metabolic syndrome showed elevated platelet aggregation and reduced platelet responsiveness to aspirin in a study of more than 2,000 people.

These findings suggest that "low-dose aspirin therapy alone may not be sufficient to provide optimal antiplatelet protection" in people with metabolic syndrome and an increased risk for coronary artery disease, Dhananjay Vaidya, Ph.D., and his associates reported in a poster at the annual scientific sessions of the American Heart Association. The link between metabolic syndrome and aspirin resistance in platelets was examined because metabolic syndrome is known to be proinflammatory and prothrombotic, they said.

The study involved 2,088 apparently healthy siblings, sibling offspring, and coparents of the sibling offspring of more than 500 patients who were younger than 60 years and hospitalized for coronary artery disease. The average age of the relatives was about 44 years, and about 58% were women. The group included 591 people (28%) who met the criteria for metabolic syndrome of the Adult Treatment Panel III guidelines of the U.S. National Cholesterol Education Program; the remaining 1,497 people (72%) did not have metabolic syndrome.

After a baseline assessment and blood collection, the subjects were treated with 81 mg/day of aspirin for 2 weeks and then were reassessed and had a second blood specimen drawn. The aggregability of each person's platelets was tested before and after aspirin treatment with two different in vitro assays. In one assay, the platelets were treated with arachidonic acid; in the second, they were treated with urinary thromboxane B_2.

Before starting aspirin, the platelets of the people with metabolic syndrome showed significantly more aggregation in both in vitro assays than the platelets from people without metabolic syndrome in an analysis that adjusted for baseline differences in age, gender, race, serum levels of LDL cholesterol and high sensitivity C-reactive protein, and smoking status, said Dr. Vaidya, a vascular researcher in the department of medicine at Johns Hopkins University, Baltimore, and his associates.

Immediately after 2 weeks of daily aspirin treatment, the platelets of the people with metabolic syndrome continued to show a significantly higher level of aggregation, compared with platelets from those without metabolic syndrome, in both assays, again in an analysis that adjusted for the same baseline differences.

The finding has clinical implications because aspirin prophylaxis for coronary artery disease is recommended for metabolic syndrome, said the researchers. ■